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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/629,895 07/30/2003 John J. Rossi 1954-413 8585

6449 7590 01/31/2007  
ROTHWELL, FIGG, ERNST & MANBECK, P.C.  
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WASHINGTON, DC 20005

EXAMINER

WHITEMAN, BRIAN A

ART UNIT

PAPER NUMBER

1635

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
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3 MONTHS

01/31/2007

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 01/31/2007.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/629,895	<b>Applicant(s)</b> ROSSI ET AL.	
	<b>Examiner</b> Brian Whiteman	<b>Art Unit</b> 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 9/6/06, 11/8/06.
- 2a) ☒ This action is **FINAL**.      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-14 is/are pending in the application.
- 4a) Of the above claim(s) 7-10 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-6 and 11-14 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>5/5/06</u> | 6) <input type="checkbox"/> Other: _____  |

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### **DETAILED ACTION**

Claims 1-14 are pending.

Applicant's traversal, the amendment to claims 1, 2, 4, 5, and 11, the addition of claims 13-14 in paper filed on 9/6/06 is acknowledged and considered by the examiner.

### ***Election/Restrictions***

Claims 7-10 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 1/30/06.

### ***Information Disclosure Statement***

The information disclosure statement (IDS) submitted on 5/5/06 was filed after the mailing date of the non-final rejection on 3/6/06. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

### ***Specification***

The disclosure remains objected to because of the following informalities: page 8 lists a US application, but the status (pending, abandoned, US patent) of the application is missing.

Appropriate correction is required.

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***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 5, 6, 11, and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rossi (AA) taken with Billy et al. (PNAS, 98: 14428-14433, 2001) and Bernstein et al. (Nature, 2001, 409:363-6). Rossi teaches incorporating a ribozyme into the loop of the VA1 promoter (loop contains a BStEII site) in an expression vector. See columns 5 and 9-10 and

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Figures 2A, 2B, and 9. Rossi teaches the limitation in claims 5 and 6. See Figures 2A and 2B.

Rossi teaches transfecting cells (stem cells) with the expression vector (columns 2 and 6).

However, Rossi does not specifically teach using RNAi in the vector, wherein the RNAi is a substrate for a mammalian Dicer.

However, at the time the invention was made, RNAi that is a substrate for a mammalian Dicer was well known to one of ordinary skill in the art as exemplified by Billy (page 14428).

In addition, at the time the invention was made, Bernstein teaches human Dicer family member is capable of generating 22 nucleotide RNAs from dsRNA substrates (page 365).

Bernstein teaches that exogenous dsRNAs can affect gene function in early mouse embryos (page 365).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Rossi taken with Billy and Bernstein, namely to produce an expression vector comprising an adenoviral VA1 promoter operatively linked to a construct comprising RNAi. One of ordinary skill in the art would have been motivated to combine the teaching to study the RNAi response in a mammalian cell in vitro.

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Rossi taken with Billy and Bernstein, namely to produce an in vitro cell comprising the expression vector comprising an adenoviral VA1 promoter operatively linked to a construct comprising RNAi. One of ordinary skill in the art would have been motivated to combine the teaching to study a gene function in a mammalian cell in vitro.

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Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments, see pages 6 and 17, filed 9/6/06, with respect to the rejection(s) of claim(s) 1-3, 5, 6, and 11-12 under 102 have been fully considered and are persuasive.

Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of the amendment to claim 1.

Claims 1, 4, and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rossi (AA) taken with Billy et al. and Bernstein et al. as applied to claims 1-3, 5, 6, 11 and 12 above, and further in view of Yu et al. (AH).

Rossi taken with Billy and Bernstein do not specifically teach using hairpin siRNA (shRNA) in the vector.

However, at the time the invention was made, Yu teaches an RNA polymerase III vector comprising shRNA can inhibit expression in mammalian cells.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Rossi, Billy and Bernstein in further view of Yu, namely to produce an RNA polymerase III vector comprising shRNA. One of ordinary skill in the art would have been motivated to combine the teaching as an economic alternative to chemical synthesis of siRNA.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments, see pages 6 and 17, filed 9/6/06, with respect to the rejection(s) of claims 1 and 4 under 103 have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of the amendment to claim 1.

NOTE: It appears the claimed invention is directed to the expression vector and not shRNA because the instant specification generically discloses shRNA (or shRNA known in the prior art) and does not claim any novel shRNA.

Claims 1, 4, and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rossi (AA) taken with Billy et al. and Bernstein et al. as applied to claims 1-3, 5, 6, 11 and 12 above, and further in view of Ambros (Cell, 2001, 107:823-6).

Rossi taken with Billy and Bernstein do not specifically teach using microRNA (miRNA) in the vector.

However, at the time the invention was made, microRNA was well known to one of ordinary skill in the art as exemplified by Ambros (pages 823-826). Ambros teaches, "Animal genomes contain an abundance of small genes that produce regulatory RNAs of about 22 nucleotides in length (abstract)." "These microRNAs are diverse in sequence and expression patterns, and are evolutionary widespread, suggesting they may participate in a wide range of genetic regulatory pathways (abstract)."

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Rossi, Billy and Bernstein in further view of

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Ambros, namely to produce the vector. One of ordinary skill in the art would have been motivated to combine the teaching to study a gene regulatory pathway in cells in vitro.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments, see pages 6 and 17, filed 9/6/06, with respect to the rejection(s) of claims 1 and 4 under 103 have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of the amendment to claim 1.

NOTE: It appears the claimed invention is directed to the expression vector and not miRNA because the instant specification generically discloses miRNA (or miRNA known in the prior art) and does not claim any novel miRNA.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.



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Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 4, 11-12, and 14 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 5, and 9 of U.S. Patent No. 6,100,087 in view of Zeng et al. Mol. Cell, 9, 1327-33, 2002. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of '087 are directed to an expression vector comprising an adenoviral VA1 promoter operatively linked to a nucleic acid encoding a ribozyme (also known as an interfering RNA molecule). The claims from '087 do not specifically recite RNAi is a substrate for mammalian Dicer.

However, at the time the invention was made, Zeng teaches that natural and designed microRNAs (miRNA) can inhibit the expression of mRNAs expressed in human cells (page 1327).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the claims of '087 with Zeng, namely to produce a vector comprising a construct encoding RNAi, wherein RNAi is a substrate for mammalian Dicer. One of ordinary skill in the art would have been motivated to produce the vector to study the RNAi in gene silencing in mammals.

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made the claims of '087 with Zeng, namely to produce a mammalian cell comprising the vector. One of ordinary skill in the art would have been motivated to produce the mammalian cell to study the RNAi in gene silencing.

Therefore the claims would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made as obvious of the claims of '087.

Applicant's arguments, see page 8, filed 11/8/06, with respect to the rejection(s) of claim(s) 1, 4, and 11-12 under have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of the amendment to claim 1.

Claims 1 and 10-11 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 7-9 of U.S. Patent No. US 6,995,258 taken with Frey et al. (Abstracts of General Meeting of the American Society for Microbiology 1992, 92, 225, H-254) in view of Zeng et al. Mol. Cell, 9, 1327-33, 2002. Claims 1 and 7-9 of '258 recite an expression cassette comprising a coding sequence for an RNA molecule an RNA pol III promoter sequence. Claim 9 recites a cell comprising the RNA molecule. One of ordinary skill in the art would understand that to express the RNA molecule in a cell the RNA pol III promoter would have to be operably linked to the RNA molecule. However, Rossi does not specifically teach using a VA1 promoter as the RNA pol III promoter to express RNAi.

However, at the time the invention was made, Frey teaches use of an adenovirus VA1 promoter in engineering antisense RNA. The ordinary skill artisan understands that a VA1 promoter is an RNA pol III promoter.

In addition, at the time the invention was made, Zeng teaches that natural and designed microRNAs (miRNA) can inhibit the expression of mRNAs expressed in human cells (page 1327).

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It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the claims of '258 taken with Frey and Zeng, namely to produce an expression cassette comprising an RNAi molecule operably linked to a VA1 promoter. One of ordinary skill in the art would have been motivated to combine the teaching to improve the stability of the RNA molecule.

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the claims of '258 taken with Frey, namely to produce a mammalian cell comprising the expression cassette comprising an RNAi molecule operably linked to a VA1 promoter. One of ordinary skill in the art would have been motivated to combine the teaching to the study the delivery of HIV TAR RNA to the nucleolus of the cell.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments, see pages 8-9, filed 11/8/06, with respect to the rejection(s) of claim(s) 1 and 10 and 11 under have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of the amendment to claim 1.

### ***Conclusion***

Claims 31-34 in co-pending US application 10/365,643 could be used in a provisional obvious type double patenting rejection with a secondary reference. However, the claims appear to be drawn to a non-elected invention. Thus, if the claims are rejoined with the elected invention, a provisional odp rejection will be applied to the instant application.

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Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP §.706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, SPE – Art Unit 1635, can be reached at (571) 272-4517.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of

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such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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Brian Whiteman

A handwritten signature in black ink, appearing to be 'B, H' or similar, written over the printed name 'Brian Whiteman'.